Personality traits and inflammation in men and women in their early 70s

RUNNING HEAD: PERSONALITY AND INFLAMMATION

Personality traits and inflammation in individuals aged around 70 and 73 years

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Abstract

Objectives: Some previous studies have reported associations between the five-factor model's (FFM) personality traits and inflammation markers interleukin-6 (IL-6) and C-reactive protein (CRP). The somewhat inconsistent associations need further replications. This study investigates the FFM personality trait–inflammation marker associations in individuals aged around 70 and 73 years. **Methods:** Participants were members of the Lothian Birth Cohort 1936 (N = 818). Acute-phase proteins—CRP and fibrinogen—were measured at ages around 70 and 73 years, and the inflammatory cytokine IL-6 was measured at age 73 years. Personality traits were measured at age 70 using two independent instruments, the International Personality Item Pool (IPIP) and the NEO Five-Factor Inventory (NEO-FFI). **Results:** Lower IPIP Conscientiousness was cross-sectionally associated with elevated CRP, such that one standard deviation higher Conscientiousness was associated with 22% lower odds of having a CRP level > 3 mg/L (OR = 0.78; 95% CI = 0.67, 0.91). Openness, as measured by the NEO-FFI, was negatively associated with CRP (OR = 0.79; 95% CI = 0.67, 0.94) and IL-6 (β = -0.08, p = 0.045) at age 73; these associations were attenuated by 26% and 63%, respectively, after adjusting for social background and prior cognitive ability. Body mass index appeared to mediate some (14%-18%) of the Conscientiousness-inflammation association, whereas common health behaviors such as smoking, alcohol consumption and physical activity did not significantly mediate the personality-trait inflammatory marker association. **Conclusion:** The findings add some support to accumulating evidence for low Conscientiousness being linked to higher levels of inflammation and poorer health in general.

KEYWORDS: Personality traits; Conscientiousness; inflammation; Interleukin-6, C-reactive protein; fibrinogen.

FFM = five-factor model; CRP = C-reactive protein; IL-6 = interleukin-6; LBC1936 = Lothian Birth Cohort 1936; SMS1947 = Scottish Mental Survey 1947; IPIP = International Personality Item Pool; NEO-FFI = NEO Five-Factor Inventory; BMI = body mass index; OR = odds ratio; CI = 95% confidence intervals; r = correlation coefficient; β = standardized regression weight from a general linear model.

Introduction

Chronic inflammation has been associated with numerous negative conditions including diabetes, cardiovascular disease, atherosclerosis and mortality (1–3), making inflammation markers valuable objective indicators of general health, especially at advanced ages (1). As will be reviewed below, some recent reports have suggested that levels of inflammation are linked to people's personality traits, which refer to tendencies in how people typically behave, think and feel and are often summarized using the five-factor model (FFM): Neuroticism (inversely called Emotional stability), Extraversion, Openness to experience (Openness; often called Intellect), Agreeableness, and Conscientiousness (4). There are good theoretical arguments for considering personality traits to be predictors of health indicators such as inflammation markers. For example, it is possible that behavioral tendencies that characterize personality traits directly contribute to people's health-related life-style choices (5) or, alternatively, moderate people's reaction to stressful situations (6).

Chapman and colleagues (7) found that low Extraversion—in particular, its activity facet—was associated with higher levels of log-transformed interleukin-6 (IL-6), an inflammatory cytokine (8), explaining about 6% of its variance. In a sample of nearly 5,000 Sardinians, Sutin and colleagues (9) found that high levels of log-transformed IL-6 were related to high Neuroticism and low Conscientiousness ($r = 0.04$ and -0.07, respectively, $p < 0.01$). Although the broad Extraversion domain was not significantly associated with IL-6, its activity facet was ($r = -0.03$, $p < 0.05$), akin to Chapman and colleagues (7). Similar, albeit weaker correlations were found for C-reactive protein (CRP), an acute-phase inflammatory protein (9). Some of the associations appeared to be mediated by smoking and body mass index

(BMI). Agreeableness and Openness were not related to inflammatory markers in this study (9).

In contrast, Jonassaint and colleagues (10) found that Openness was the only FFM personality trait that was significantly related to CRP levels. Although this association was observed only among black participants, it was notably stronger (r = -0.41) than results from other studies. Chapman and colleagues (11) also found that Openness along with Conscientiousness predicted the levels of IL-6 across three measurements taken over a period of 34 weeks. The associations were to a small extent accounted for by various health-related behaviors and chronic health conditions. The reviewed findings are summarized in Table 1.

Table 1 about here

Possible explanations for this somewhat inconsistent pattern of associations include relatively small ($N \leq 200$) samples—except for the study by Sutin and colleagues (9)—and their demographic diversity, with stronger associations appearing in individuals aged 65 years or older (9,11) or in people of specific ethnic backgrounds (10). The Openness-inflammation associations may also have been confounded by cognitive ability, which tends to correlate positively with Openness (12) and negatively with inflammation, as demonstrated in the same sample that will be used in this study (13,14) and elsewhere (15). Therefore, further studies with sufficiently large samples and the availability of potentially important co-variates are needed to document the personality-inflammation associations.

With this in mind, the present study tests cross-sectional and longitudinal (over 3 years) associations between FFM personality traits as measured by two different instruments and

three inflammatory markers in a relatively large sample (N = 818) of people aged around 70 years at the first assessment, the Lothian Birth Cohort 1936 (LBC1936). Investigating the associations at this age is especially meaningful as inflammation and its health correlates are more prevalent and the effects of life-course risks of poor health may have accumulated. With three inflammatory markers that reflect different aspects of inflammatory processes, the study adopts a comprehensive approach to inflammation. IL-6 is an up-stream marker that stimulates the immune response by induction of acute-phase protein production by the liver (16). As a more down-stream marker, acute-phase protein CRP is a component of the innate immune system, whose roles include activation of the complement system (8). Fibrinogen, a component of the blood coagulation cascade and a determinant of blood viscosity, is a more peripheral marker of inflammation (16).

Based on the few previous studies (particularly the large-sample Sardinian study, 9), we expect low Emotional stability and Conscientiousness to be the significant cross-sectional and longitudinal correlates of higher levels of inflammatory markers. We also hypothesize that lower Openness (Intellect) will be correlated with higher inflammatory marker levels (10,11), with the effect possibly being confounded by life-long cognitive ability. We additionally control for other potential life-course factors such as educational level and occupational class that may contribute to individual differences in both inflammation (17) and personality traits (18) and therefore confound their association. The effect sizes are expected to be small. We hypothesize that Extraversion and Agreeableness will not be associated with inflammatory markers. With no clear reasons to suggest otherwise, the

associations are expected to generalize across personality instruments and inflammatory markers.

We also consider possible mediating pathways that could link personality traits and inflammation. Neuroticism and Conscientiousness are associated with health-related behaviors such as smoking, alcohol use or physical activity (19–21), which in turn may relate to inflammatory processes (9). We also consider the possible mediating role of body mass index, which has been associated with Conscientiousness and Neuroticism (22), and inflammatory markers (14,23). The conceptual mediation model is depicted in Figure 1.

Figure 1 about here

Method

Participants

The Lothian Birth Cohort 1936 (LBC1936) is a study of healthy aging. Between 2004 and 2007, 1,091 surviving participants (548 males) of the Scottish Mental Survey 1947 (24) were recruited to the study. Full details on the background of the study, recruitment process, measures, and procedures are available elsewhere (25). At this first wave of old-age testing, they varied in age from 67.7 to 71.3 years. All were living independently in the community. About three years later (henceforth referred to as age 73), 866 participants who were able and agreed to continue in the study were re-tested in the course of a comprehensive follow up study (25). The current study uses a subsample of LBC1936 participants with the inclusion conditions being the presence of data on at least one personality trait and inflammatory marker combination and all co-variates, and the absence of acute inflammation (CRP < 10

mg/L; to omit possible acute illness) in at least one testing occasion. For full details on the subsample used in this study see Table 2. Ethics permissions for the study were obtained from the Multi-Centre Research Ethics Committee for Scotland.

Measures

Personality traits (at age 70). Traits were measured with the 50-item International Personality Item Pool (IPIP) (26), which has ten items for each of the five FFM personality traits: Emotional stability, Extraversion, Agreeableness, Conscientiousness, and Intellect (broadly similar to Openness as measured in other FFM questionnaires such as the NEO Five-Factor Inventory [NEO-FFI]; 27). Participants rated each item on a 5-point Likert-type scale ('very inaccurate' (0) to 'very accurate' (4)). In parallel, personality traits were measured with the NEO-FFI (27), a 60-item measure that has 12 items for each of the five FFM personality traits, rated on a similar 5-point Likert-type scale. The Neuroticism scores of the NEO-FFI were reversed, so that they also reflected Emotional stability.

Inflammatory markers (at ages 70 and 73). Blood samples were taken to estimate participants' plasma CRP (mg/L) and fibrinogen levels (g/L) at ages 70 and 73, and IL-6 (pg/mL) at age 73. The CRP assay was performed using a dry-slide immuno-rate method on the OrthoFusion 5.1 F.S analyzers. The method has low sensitivity in the lower range of CRP values; therefore, about 55% of the participants at age 70, and 59% at age 73 fell into a single lowest category (1.5 mg/L). Therefore, for the main analyses, all CRP values were collapsed into two categories: $\leq$ 3 mg/L (normal, including the measured values of 1.5 mg/L and 3 mg/L) and >3 mg/L (elevated; including the rest of the values). Besides being meaningful for

the current distribution of CRP values, the relevance of the 3 mg/L cutoff has been suggested for cardiovascular disease prediction (28). Some additional analyses are presented whereby CRP is treated as a log-transformed variable. Fibrinogen was measured using an automated Clauss assay (TOPS coagulometer, Instrumentation Laboratory, Warrington, UK). IL-6 was determined using high-sensitivity ELISA kits (R&D Systems, Oxon, UK). The distribution of IL-6 values was initially skewed but close to normal after log-transformation.

Covariates

Social and cognitive background variables. Highest level of educational attainment was represented with five categories ranging from 'no qualification' (0) to 'degree' (4). Occupational class prior to retirement was captured on a six-point scale ranging from manual labor (1) to professional (6) (29). Women with a lower occupational class than their spouse were classified according to their spouse. As a measure of childhood intelligence, scores from the Moray House Test taken at age 11 were used (24,25). The scores were standardized at the level of the whole LBC1936 follow-up sample (N = 1,091; mean = 100, standard deviation = 15).

Health co-variates (ages 70 and 73). The presence of at least one of the following self-reported health conditions was recorded: high blood pressure, diabetes, arthritis, cancer, and histories of CVD and stroke. Additionally, forced expiratory volume in 1 sec (FEV1) was used as a general physical fitness indicator. FEV1 was measured using a microspirometer; the best of three trials was recorded.

Health-related behavior (at ages 70 and 73). Participants were asked whether they were current smokers (coded as 2), ex-smokers (1) or had never smoked (0). They also reported average weekly alcohol intake as the type and quantity of alcohol consumed, which was then converted into alcohol unit equivalents. To account partially for possible non-linear role of alcohol consumption, participants were categorized as non-drinkers (0 units per day), low-level drinkers (≤ 2 units per day), or moderate to substantial drinkers (> 2 units per day), as has been done previously (30). Physical activity (measured only at age 70) was recorded on a six-point scale ranging from 'household chores' (1) to 'heavy exercise several times a week' (6). Body mass index (BMI, kg/m2) was calculated using height and weight measured at the research clinic. Smoking and alcohol use were treated as ordered categorical and physical activity and BMI as continuous variables in mediation analyses.

Statistical analyses

All analyses were carried out in R (2.15) statistical software (31). For CRP (elevated versus normal), a series of logistic regressions was carried out. First, CRP at ages 70 and 73 years were predicted by the five personality traits (separately) along with sex and age at the time of CRP measurement. Then, to control for the possible confounding/mediating effects of social and cognitive background, educational level, occupational class, and childhood cognitive ability scores were added to the model as predictors for those personality traits that had at least one significant association with CRP in the previous type of model. Next, to account for possible confounding/mediating effects of general health condition, a binary co-variate representing the presence of any of the above-mentioned health conditions and FEV1 were added to the regression. For fibrinogen and IL-6, similar analyses were carried out with the

only exception being that linear regression was used. Regardless of the co-variates included, all models for particular personality trait-inflammation marker combinations were tested on the same set of people.

We investigated whether personality traits were associated with changes in inflammatory marker levels over 3 years, including only those people who did not have acute inflammation (defined as CRP > 10 mg/L) at any of the two time points (N = 567). First, changes in CRP were calculated as differences in categories (normal vs elevated). If people fell into the same category at both testing occasions they were considered to have not changed in terms of CRP (coded as 0; N = 359). If a person had a CRP level in the normal range at first testing occasion but elevated level at the second testing occasion, and the increase in raw CRP level had been larger than 25% of the initial level, then he or she was considered as having increased in terms of CRP (coded as 1; N = 91). Conversely, if a person had an elevated CRP at first testing occasion but a normal level at the second testing occasion, and the decline in raw CRP level had been larger than 25% of the initial level, then he or she was considered as having a decreasing CRP over time [coded as (-1); N = 117]. Additionally, log-transformed raw CRP values at age 73 were residualized for log-transformed values at age 70 to obtain a complementary index of CRP change. In order to quantify changes in fibrinogen, its levels at age 73 were residualized for its levels at age 70.

Finally, we tested the extent to which the associations still significant after co-variate adjustment were mediated by smoking, alcohol use, physical activity, and BMI. We used the Causal Mediation Analysis (32) as implemented in the R-package ‘mediation’ (version 4.1; 33). We used nonparametric bootstrap estimation with 1,000 re-samplings. In the mediation

analyses, we adjusted for all co-variates. Smoking status and alcohol use were modeled using probit link, whereas physical activity level and BMI were modeled via linear regression. Personality traits scores and fibrinogen and log-transformed IL-6 values were standardized (z-scores) before mediation analyses: for predictors, 0 was taken as 'control' value and 1 as 'treatment' value.

Because the effect sizes were expected to be small (9) and we sought to replicate previous findings rather than reject null hypothesis, we used the 5% alpha level as a criterion of statistical significance. We acknowledge (and address in Discussion) the possibility that, due to multiple testing, this criterion might result in a number of Type I errors.

Results

Descriptive statistics are given in Table 2. The cross-sectional correlations between CRP and fibrinogen were $\beta = 0.24$ ($p < 0.001$) at age 70 and $\beta = 0.32$ ($p < 0.001$) at age 73. At age 73, log-transformed IL-6 (logIL-6) was associated with CRP and fibrinogen, respectively, $\beta = 0.34$ and $r = 0.27$ ($p < 0.001$). Longitudinal (over three years) correlations were r (polychoric) = 0.34 ($p < 0.001$) for CRP and $r = 0.53$ ($p < 0.001$) for fibrinogen. Fibrinogen changes over 3 years were correlated at r (rank-order) = 0.21 ($p < 0.001$) with the categorical and $r = 0.07$ ($p = 0.14$) with the residuals-based changes in CRP [the latter two were correlated at r (rank-order) = 0.79, $p < 0.001$]. The corresponding IPIP and NEO-FFI scores were correlated as follows ($p < 0.001$ for all): 0.79 (Emotional Stability), 0.62 (Extraversion), 0.59 (Openness/Intellect), 0.56 (Agreeableness), and 0.75 (Conscientiousness).

For comparability with previous studies, unadjusted correlations between personality scores and inflammation markers are given in Table 3 (CRP is treated both as binary and log-transformed variable). In the following, however, we will focus on the associations that are, at a minimum, adjusted for sex and age at the time of inflammation marker assessment.

Table 2 to 3 about here

Cross-sectional relationships

At age 70, one standard deviation higher IPIP-based Conscientiousness was associated with 22% lower odds of having elevated CRP [odds ratio (OR) = 0.78, p = 0.002, 95% confidence intervals (CI) 0.67, 0.91; Table 4]. The association (OR) was slightly (10%) attenuated after controlling for the presence of a disease and lung function (OR = 0.80, p = 0.004, CI 0.68, 0.93). NEO-FFI Conscientiousness scores were not significantly (p = 0.11) associated with CRP. Fibrinogen at age 70 was associated with NEO-FFI Agreeableness (β = -0.08, p = 0.04; Table 5) but the association was attenuated by 13% and fell short of significance after full co-variate adjustment (β = -0.07, p = 0.07).

Tables 4 to 5 about here

Longitudinal relationships

Higher NEO-FFI Openness (but not the IPIP Intellect) at age 70 was associated with lower age-73 CRP (OR = 0.79, p = 0.009, CI 0.67, 0.94; Table 4) and logIL-6 (β = -0.08, p = 0.045; Table 6). Controlling for social and cognitive background, presence of common disease and lung function slightly (16%) attenuated the association of the Openness with CRP (OR =

0.82, p = 0.04, CI 0.68, 0.99), whereas the attenuation was more substantial (50%) for logIL-6 (β = -0.04, p = 0.36). Higher Conscientiousness as measured with both the IPIP and the NEO-FFI was (borderline) significantly linked with lower logIL-6 (respectively β = -0.10, p = 0.02, and -0.08, p = 0.06). Adjusting for the presence of a common disease and lung function attenuated (30% to 38%) the associations (β = -0.07, p = 0.08, for the IPIP and β = -0.05, p = 0.21, for the NEO-FFI). Finally, higher NEO-FFI Emotional Stability was linked to lower logIL-6 (β = -0.09, p = 0.04) but this association was attenuated (44%) after co-variate adjustment (β = -0.05, p = 0.21).

Table 6 about here

Interaction with sex, intelligence, educational level and occupational class

Next, we tested whether any personality trait-inflammatory marker association were moderated by sex, childhood intelligence, educational level or social class. We considered only those interactions for which the interaction terms of personality trait-inflammatory marker associations replicated significantly (p < 0.01) across two testing waves, personality instruments or inflammatory markers, because testing for these interactions involved a large number (200) of statistical tests and, unlike the main effects, no clear hypotheses could be formed based on previous literature as to which interactions to expect. Based on these criteria, no significant interactions were found.

Possible mediating roles of health-behaviors and body weight

The cross-sectional association between the IPIP Conscientiousness and CRP was not significantly mediated by smoking status (the proportion of total effect via mediation 1.6%),

alcohol use level (6.9%) or physical activity (5.0%), whereas the association was significantly mediated by BMI (18.3%). Here, 'significance' means that the 95% confidence intervals of the indirect effect did not include zero. The longitudinal association between NEO-FFI Openness and CRP was not significantly moderated by smoking status (2.2%), alcohol use level (0.9%), physical activity (5.0%), or BMI (1.2%).

Although the longitudinal association between the IPIP-based Conscientiousness and logIL-6 fell slightly short of statistical significance after covariate-adjustment, we tested the degree of mediation. None of the mediation effects were significant although there was, again, a trend for BMI: the values were 6.9% for smoking status, 2.6% for alcohol use level, 8.9% for physical activity, and 14.4% for BMI.

Changes in inflammation

Unadjusted correlations between personality scores and changes in inflammation marker levels are given in Tables 7. To control for age and sex, the associations between personality traits and categorical CRP changes [coded as -1 for decline, 0 for no change and 1 for increase] were also investigated with probit regression. None of the IPIP or NEO-FFI personality trait scores was significantly associated with CRP changes [p-values ranged from 0.08 to 0.91, with a median of 0.30; the positive univariate association between NEO-FFI Conscientiousness and CRP change (Table 7) was attenuated by 32% after controlling for age and sex and was no longer significant, $p = 0.10$]. Additionally, the associations with residuals-based CRP changes were tested with linear regressions. Controlling for age and sex, only NEO-FFI Openness was significantly associated with changes in CRP ($\beta = -0.10$, $p =$

0.01). This association was attenuated by 20% after adjusting for childhood cognitive ability, education and occupational class (β = -0.08, p = 0.07) and 10% attenuated after additionally adjusting for the presence of a disease and lung function (β = -0.09, p = 0.050).

The associations between personality traits and changes fibrinogen levels over 3 years were investigated with linear regression. Controlling for age and sex, none of the personality trait scores was significantly associated with fibrinogen changes (p-values ranged from 0.07 to 0.90, with a median of 0.57).

Table 7 about here

Discussion

The study investigated associations between the FFM personality traits, as measured by two different instruments, and three inflammation markers in a relatively large sample of people aged around 70 years at the first assessment. Based on the few previous studies, we expected low Emotional stability, Openness/Intellect and Conscientiousness to be significant correlates of higher levels of inflammation markers, with the effect of Openness/Intellect possibly being confounded by people's social and cognitive background. These hypotheses were to some extent corroborated by the data. Low Conscientiousness as measured by one instrument (IPIP) but not the other (NEO-FFI) was cross-sectionally associated with higher CRP. Low Conscientiousness as measured by both instruments was longitudinally associated with higher IL-6 but this association was attenuated and no longer significant after adjustment for general health condition. Lower Intellect as measured with the NEO-FFI was longitudinally associated with higher CRP and IL-6, and these associations, especially for IL-6, were

attenuated after adjustment for social and cognitive background variables. As hypothesized, Extraversion and Agreeableness were not significantly associated with any of the inflammatory markers after co-variate adjustments.

Discovering the associations between personality traits and inflammatory markers—and potentially other objective health-markers—is made difficult by the presumably small effect sizes. Theoretically, it may be realistic to expect a single predictor to explain, say, 1% or even less variance in a health indicator that is likely to have myriad determinants with complex interactions. In practical terms, reliable discovery of such effects requires either very large samples or numerous studies on smaller samples reporting consistent results. To date, only one study has tested the associations between personality traits and inflammatory markers in a large sample (9) and, indeed, it demonstrated very small, albeit statistically significant, associations. The other studies have been carried out on smaller samples (7,10,11). Therefore, studies that could either replicate the associations—or consistently fail to do so—were (and still are) needed. The present findings provide some confirmatory evidence for personality traits being associated with inflammatory processes. Although only a limited number of statistically significant associations appeared, linking primarily Conscientiousness and Intellect with inflammation made them consistent with the previous findings. This makes it less likely that these few significant associations reflected merely type I errors, although this still remains possible. Nevertheless, we stress that further studies that attempt to replicate the associations are needed before any definitive conclusions can be drawn.

According to the present results, the previously-reported associations between Openness and inflammatory processes (10,11) may have been to some extent confounded by people's

cognitive and socioeconomic backgrounds. Significant associations between Openness and levels of inflammatory markers, where they appeared, were attenuated after adjusting them for educational level, occupational class, and childhood intelligence. This is consistent with the possibility that the personality trait Openness relates to inflammation to some extent because it is a co-variate of cognitive ability (12), which has been found to be a predictor of inflammation (13,15). None of the previous studies has been able to test the possible confounding effect of prior cognitive ability.

Adjusting the associations of Conscientiousness with IL-6—and to some extent also CRP—for general health condition (presence of a disease and lung function) had an attenuating effect, which suggests that the personality trait tended to be associated with health status more generally than merely inflammation. This is in line with the increasingly well documented links between Conscientiousness and health (34). However, this attenuating effect raises two questions. First, with inflammation being associated with many adverse health conditions, it might be questioned whether stripping the personality trait-inflammation associations from variance related to general health status is not over-correcting; that is, it is possible that elevated levels of inflammatory markers without worsened health in general is an unlikely situation to posit. Alternatively, the health conditions captured by the presence of diseases and lung function might be seen as mediators in the personality trait-inflammation associations (for a discussion between confounding and mediation, see 35). If either of these lines of reasoning is true, then the personality-trait inflammation associations that were *not* adjusted for general health conditions can be seen as the estimates of total effect.

There was only modest evidence for the associations between Conscientiousness or Openness and inflammatory markers being mediated by common health-related behaviors such as smoking, alcohol use or level of physical activity, which are some of the popular candidate mediators for the links between Conscientiousness and health status (5). This finding is consistent with some (11) but not all of the previous studies (9). However, Conscientiousness had a significant indirect negative association with CRP via BMI (with 18% of the total association being mediated) and there was a similar tendency for logIL-6, meaning that BMI may to some extent mediate Conscientiousness-inflammation associations. This is consistent with Conscientiousness being an established predictor of obesity (9), which in turn may regulate inflammatory processes (23). However, BMI did not completely mediate the Conscientiousness-inflammation associations. Alternative pathways may include adherence to medical advice and medication plans (36). We note that the personality-inflammation associations were cross-sectional, or longitudinal over only a 3-year period, such that any evidence of potential mediation or causality could only be suggestive.

There were differences between the two personality instruments in how their Openness/Intellect and Conscientiousness scores were associated with inflammatory markers. In particular, IPIP Conscientiousness and NEO-FFI Openness had slightly stronger links with inflammatory markers than the NEO-FFI Conscientiousness and IPIP Intellect, respectively. A comparison the Conscientiousness items of IPIP and NEO-FFI shows that the former focuses mainly on being orderly and self-disciplined, whereas the latter also taps being dutiful and achievement-oriented. Therefore, it may be that the order and self-discipline aspects of Conscientiousness are somewhat stronger correlates of inflammation than some

other aspects. Comparing the Intellect items of IPIP and Openness items of the NEO-FFI reveals that the former focuses mainly on being cognitively active and able, while the latter also measures behavioral expressions of intellectual curiosity (interests in arts and poetry) and tolerance. More detailed research at the facet and item levels of these traits is warranted in health psychology research.

Previous research on the association between personality traits and inflammation has focused on the cytokine IL-6 and the acute-phase protein CRP, whereas other inflammatory markers such as fibrinogen have not been considered. The present study did not provide any evidence for fibrinogen being associated with personality traits. This may be because fibrinogen, being a protein implicated in blood coagulation, is a more peripheral (and somewhat less sensitive) marker of inflammation (2,16).

The strengths of the present study include a relatively large sample aged around 70 years at the first assessment, the narrow range of ages (which minimizes the influence of chronological age as a confounder), the availability of longitudinal data, multiple markers of inflammatory processes and multiple measures of personality, and potentially important confounding variables including prior cognitive ability. A limitation is not having more detailed information on participants' personality traits. Specifically, in the present study the FFM traits were measured at the level of the broad domains, whereas more specific aspects of the broad personality traits (i.e. facets) may have different, stronger and potentially more informative associations with inflammatory markers (7,9). In addition, the results here clearly apply to the narrow age range and specific cultural group that the study represents (i.e., the cohort effect). Finally, the sample represented the healthier part of age the age-group (even

more so at the second testing), which might have led to underestimation of the effects due to restricted variance in key measures.

To conclude, there appear to be small but somewhat recurring associations between the personality trait Conscientiousness and inflammation markers. Describing the personality correlates of elevated inflammatory markers is potentially important for at least three reasons. First, levels of inflammatory markers are predictive of a range of common adverse health outcomes (16). Therefore, the finding that inflammatory processes are associated with a personality trait implies the potential involvement of this trait in a wide range of common health conditions. Second, the associations between personality traits and inflammatory markers may be informative about the mechanisms that link personality traits to other health conditions that are related to inflammation (e.g., various cardiovascular problems). The third potential implication is practical: if individuals with low Conscientiousness are more susceptible to heightened levels of inflammatory processes—which in turn are related to various adverse health outcomes—then this information, among others, can be used to identify individuals at risk of developing a range of adverse health conditions, as has been discussed at length elsewhere (37).

Future directions may involve looking for possible moderators of the associations between low Conscientiousness and elevated inflammatory marker levels. For example, the role of personality traits may be stronger for individuals who are, due to some genetic or environmental reasons, at high risk for conditions that involve elevated inflammation.

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Table 1. Summary of the previous findings on personality-inflammatory marker associations.

	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
Chapman et al. (7) (N = 103; log-transformed IL-6)	0	–	NA	NA	NA
Sutin et al. (9) (N = 4923; log-transformed IL-6 & CRP)	+	0	0	0	–
Jonassaint et a. (10) (N = 165; CRP)	0	0	– (only African Americans)	0	0
Chapman et al. (11) (N = 200; IL-6)	0	0	–	0	–

NOTE: N = number of participants; IL-6 = interleukin-6; CRP = C-reactive protein; NA = not applicable (not tested); + = positive association; – = negative association; 0 = no association. Because different studies used different effect size metrics, effect sizes are not directly comparable.

Table 2. Descriptive statistics of the study variables.

	Age 70			Age 73			r	α
	N	Mean (%)	SD	N	Mean (%)	SD		
Age	818	69.52	0.85	685	72.52	0.73		
Female	411	50.2%		336	49.1%			
Emotional stability (IPIP; age 70)	808	24.82	7.69	676	25.07	7.67		0.88
Extraversion (IPIP; age 70)	811	21.32	7.12	679	21.22	7.12		0.85
Intellect (IPIP; age 70)	805	23.95	5.76	675	23.96	5.77		0.75
Agreeableness (IPIP; age 70)	808	31.11	5.35	677	31.05	5.38		0.80
Conscientiousness (IPIP; age 70)	808	28.28	5.99	676	28.17	6.02		0.78
Emotional stability (NEO-FFI; age 70)	810	16.94	7.61	680	16.75	7.59		0.87
Extraversion (NEO-FFI; age 70)	804	27.00	5.89	673	27.03	5.86		0.79
Openness	807	26.24	5.76	676	26.35	5.85		0.72

(NEO-FFI; age 70)								
Agreeableness (NEO-FFI; age 70)	812	33.42	5.21	680	33.49	5.21		0.74
Conscientiousness (NEO-FFI; age 70)	806	34.66	6.03	674	34.60	6.19		0.86
C-reactive protein (mg/L)	806			661			0.34	
Normal (≤ 3 mg/L)	440	54.6%		392	59.3%			
Elevated (> 3 mg/L)	366	45.4%		269	40.7%			
Fibrinogen (g/L)	808	3.25	0.62	651	3.30	0.58	0.53	
Interleukin-6 (pg/mL)				648	1.87	1.48		
Age 11 cognitive ability	818	101.16	14.48	685	101.48	14.88		
Educational attainment	818	1.73	1.31	685	1.76	1.33		
occupational class	818	2.33	0.91	685	2.32	0.91		
Smoking status:	818			685			0.92	
Current smoker	92	11.6%		49	7.2%			
Quitted smoker	361	44.1%		307	44.8%			
Never smoker	362	44.3%		329	48.0%			
Drinking status	818			685			0.79	

Non-drinker	145	17.7%		156	22.8%		
Low-level drinker	149	18.2%		121	17.7%		
Moderate/substantial drinker	524	64.1%		408	59.5%		
Physical activity (age 70)	818	2.99	1.08	685	3.03	1.07	
Body mass index (kg/m^2)	818	27.54	4.18	685	27.58	4.20	0.94
Forced expiratory volume (L/sec)	818	2.40	0.68	685	2.31	0.66	0.93
Presence of common disease	818			685			0.64
Yes	620	75.8%		563	82.1%		

NOTE: SD = standard deviation; r = stability over time (Pearson correlation for continuous variables, polychoric correlation for ordinal-categorical variables; $p < 0.001$ for all); α = Cronbach's alpha. Fibrinogen and forced expiratory volume levels differed significantly (paired t-test) over time ($p = 0.04$ and $p < 0.001$) but not body mass index ($p = 0.06$). Distributions of C-reactive protein and smoking status did not differ significantly over time for people with complete data at both testings (according to the test for equality of proportions; $p = 0.07$ and 0.11, respectively), whereas the distributions of drinking status and the presence of disease did differ significantly (respectively $p = 0.03$ and $p < 0.001$).

Table 3. Unadjusted correlations of the FFM personality traits measured at age 70 with inflammatory markers measured at ages 70 and 73.

	CRP at age 70 (bin)		CRP at age 70 (log)		CRP at age 73 (bin)		CRP at age 73 (log)		Fibrinogen at age 70		Fibrinogen at age 73		IL-6 at age 73 (log)	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p
IPIP (age 70)														
Emotional stability	-0.03	0.42	-0.03	0.49	-0.08	0.049	-0.07	0.09	0.03	0.46	0.06	0.14	-0.07	0.09
Extraversion	-0.06	0.12	-0.03	0.42	-0.02	0.62	-0.02	0.56	-0.03	0.37	-0.02	0.57	0.00	0.93
Intellect	-0.04	0.25	-0.04	0.26	-0.05	0.25	-0.08	0.07	-0.02	0.66	-0.04	0.36	-0.01	0.83
Agreeableness	-0.03	0.36	-0.04	0.29	-0.05	0.22	-0.08	0.04	-0.04	0.34	-0.01	0.80	-0.09	0.03

Conscientiousness	-0.13	< 0.001	-0.12	< 0.001	-0.08	0.06	-0.09	0.03	0.00	0.91	-0.02	0.58	-0.12	0.003
NEO-FFI (age 70)														
Emotional stability	0.04	0.24	0.04	0.29	0.07	0.11	0.07	0.07	0.03	0.46	0.00	0.96	0.10	0.02
Extraversion	-0.05	0.17	-0.03	0.44	0.02	0.57	0.02	0.60	-0.05	0.16	-0.01	0.75	-0.02	0.67
Openness	-0.08	0.03	-0.08	0.04	-0.10	0.02	-0.10	0.01	0.00	0.95	-0.05	0.27	-0.09	0.02
Agreeableness	-0.05	0.14	-0.04	0.25	-0.06	0.14	-0.10	0.02	-0.05	0.20	-0.03	0.43	-0.10	0.02
Conscientiousness	-0.07	0.054	-0.06	0.10	0.00	0.91	-0.03	0.51	0.02	0.61	0.00	0.91	-0.11	0.009

NOTE: IPIP = International Personality Item Pool; NEO-FFI = NEO Five-Factor Inventory; CRP = C-reactive protein; bin = binary variable (CRP ≤ 3 mg/L vs CRP > 3 mg/L); log = log-transformed variable; r = correlation coefficient. All correlations involving CRP are Spearman rank-order correlations. All other correlations are Pearson zero-order correlations.

Table 4. Adjusted cross-sectional and longitudinal associations between personality and C-reactive protein (CRP).

	Age 70 (cross-sectional associations)				Age 73 (longitudinal associations)			
	IPIP N = 749 – 754		NEO-FFI N = 748 – 756		IPIP N = 613–616		NEO-FFI N = 611–617	
	OR [CI]	p	OR [CI]	p	OR [CI]	p	OR [CI]	p
	A. Controlling for age and sex							
Emotional stability	0.96[0.82;1.11]	0.57	0.93[0.80;1.08]	0.35	0.86[0.72;1.01]	0.07	0.89[0.75;1.05]	0.16
Extraversion	0.89[0.76;1.03]	0.11	0.88[0.76;1.02]	0.09	0.91[0.77;1.08]	0.27	1.00[0.85;1.19]	0.98
Openness/Intellect	0.94[0.81;1.09]	0.42	0.89[0.77;1.04]	0.15	0.87[0.73;1.03]	0.10	0.79[0.67;0.94]	0.009

Agreeableness	0.91[0.78;1.07]	0.25	0.88[0.76;1.03]	0.12	0.94[0.78;1.12]	0.47	0.85[0.71;1.01]	0.06
Conscientiousness	0.78[0.67;0.91]	0.002	0.88[0.76;1.03]	0.11	0.91[0.76;1.07]	0.24	1.01[0.85;1.19]	0.95
B. A + controlling for social and cognitive background								
Openness/Intellect	1.02[0.87;1.20]	0.82	0.98[0.83;1.15]	0.79	0.92[0.77;1.10]	0.38	0.84[0.70;1.01]	0.06
Conscientiousness	0.78[0.67;0.90]	0.001	0.87[0.75;1.01]	0.07	0.90[0.76;1.07]	0.22	0.99[0.84;1.18]	0.92
C. B + controlling for chronic diseases and lung function								
Openness/Intellect	0.99[0.84;1.17]	0.91	0.97[0.82;1.14]	0.69	0.93[0.77;1.11]	0.41	0.82[0.68;0.99]	0.04
Conscientiousness	0.80[0.68;0.93]	0.004	0.89[0.76;1.04]	0.14	0.96[0.80;1.14]	0.62	1.06[0.89;1.26]	0.53

NOTE: The results are obtained using logistic regression models. Social and cognitive background includes educational level, occupational class and childhood cognitive ability. OR = odds ratio; CI = 95% confidence intervals.

Table 5. Adjusted cross-sectional and longitudinal associations between personality and fibrinogen.

	Fibrinogen at age 70 (cross-sectional associations)				Fibrinogen at age 73 (longitudinal associations)			
	IPIP		NEO-FFI		IPIP		NEO-FFI	
	N = 742 – 747		N = 741 – 749		N = 598–600		N = 595–602	
	β	p	β	p	β	p	β	p
	A. Controlling for age and sex							
Emotional stability	0.03	0.38	-0.02	0.61	0.08	0.05	0.02	0.60
Extraversion	-0.04	0.33	-0.05	0.15	-0.05	0.27	-0.02	0.58
Openness/Intellect	-0.02	0.51	-0.01	0.70	-0.07	0.07	-0.06	0.13
Agreeableness	-0.07	0.07	-0.08	0.04	-0.02	0.64	-0.03	0.43
Conscientiousness	-0.02	0.64	0.00	0.92	-0.03	0.46	0.00	0.94

			B. A + controlling for social and cognitive background					
Agreeableness	-0.07	0.09	-0.07	0.05	-0.03	0.51	-0.03	0.47
			C. B + controlling for chronic diseases and lung function					
Agreeableness	-0.07	0.07	-0.07	0.07	-0.02	0.57	-0.02	0.68

NOTE: The results are obtained using linear regression models. Social and cognitive background includes educational level, occupational class and childhood cognitive ability. β = standardized regression coefficient.

Table 6. Adjusted longitudinal associations between personality and log-transformed interleukin-6 (logIL-6).

	Interleukin 6 at age 73			
	IPIP		NEO-FFI	
	N = 594 – 597		N = 592 – 599	
	β	p	β	p
	A. Controlling for age and sex			
Emotional stability	-0.06	0.15	-0.09	0.04
Extraversion	0.02	0.71	-0.01	0.86
Openness/Intellect	0.00	0.93	-0.08	0.045
Agreeableness	-0.05	0.27	-0.08	0.08

Conscientiousness	-0.10	0.02	-0.08	0.06
B. A + controlling for social and cognitive background				
Emotional stability	-0.04	0.38	-0.07	0.12
Openness/Intellect	0.05	0.21	-0.03	0.78
Conscientiousness	-0.10	0.01	-0.08	0.046
C. B + controlling for chronic diseases and lung function				
Emotional stability	-0.02	0.59	-0.05	0.21
Openness/Intellect	0.05	0.20	-0.04	0.36
Conscientiousness	-0.07	0.08	-0.05	0.21

NOTE: The results are obtained using linear regression models. Social and cognitive background includes educational level, occupational class and childhood cognitive ability. β = standardized regression coefficient.

Table 7. Unadjusted correlations of the FFM personality traits measured at age 70 with changes in inflammatory markers between ages 70 and 73.

	CRP change (categorical)		CRP change (residualized)		Fibrinogen change (residualized)	
	r	p	r	p	r	p
IPIP (age 70)						
Emotional stability	-0.05	0.20	-0.06	0.18	0.03	0.50
Extraversion	0.02	0.69	0.00	0.98	-0.03	0.43
Intellect	-0.01	0.88	-0.05	0.27	-0.03	0.45
Agreeableness	-0.01	0.81	-0.04	0.37	0.02	0.65
Conscientiousness	0.06	0.14	-0.01	0.80	0.01	0.85

NEO-FFI (age 70)						
Emotional stability	0.02	0.65	0.03	0.56	-0.01	0.75
Extraversion	0.06	0.14	0.07	0.09	0.01	0.83
Openness	-0.03	0.42	-0.07	0.12	-0.07	0.13
Agreeableness	0.03	0.48	-0.05	0.24	0.00	0.97
Conscientiousness	0.09	0.03	0.04	0.33	0.03	0.54

NOTE: IPIP = International Personality Item Pool; NEO-FFI = NEO Five-Factor Inventory; CRP = C-reactive protein; r = correlation coefficient. All correlations involving CRP changes are Spearman rank-order correlations, whereas others are Pearson zero-order correlations. See Methods for information on how the change estimates were calculated.

Figure 1. Conceptual mediation model between personality traits and inflammation markers.